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CONTRACT NO: DAMD17-85-C-5133

TITLE: PHASE I CLINICAL PHARMACOLOGY STUDIES

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Description of progress under Task Order #7, #8, #9, #10, #11, #12, #13, and #14.

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SUMMARY

This annual report contains a listing of the task orders and work performed on each during the period of March 9, 1989 through August 31, 1990 for Contract No. DAMD17-85-C-5133.

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Foreword

Citations of commercial organizations and trade names in this report do not constitute an official Department of the Army endorsement or approval of the products or services of these organizations.

For the protection of human subjects the investigators have adhered to policies of applicable Federal Law 45CFR46.

Body of Report

During this period of the contract, our group worked on the following Task Orders:

1. Task Order #7

Title: "Pharmacokinetics and Pharmacodynamics of Sustained, Low-dose, Intravenous Infusions of Pyridostigmine"

The clinical portion was conducted between July 27, 1987 and October 16, 1987 and, thus, had already been completed prior to this reporting period. Evaluation of the data continued.

2. Task Order #8

Title: "Safety, Tolerance, Pharmacokinetics and Pharmacodynamics of Single Oral Doses of Sustained-release Pyridostigmine in Healthy Men"

The clinical portion was initiated on January 11, 1988 and was completed on April 23, 1988. The preparation of the task report was under way during this reporting period. Draft task reports and copies of our case report forms for this study were sent to the Contracting Officer Representative (COR), Col. Brian G. Schuster, for his review and review by other selected Army personnel. Revisions in the drafts were made based on their review and discussions with our group.

3. Task Order #9

Title: "Safety, Tolerance, Pharmacokinetics and Pharmacodynamics of Single Oral Doses of Sustained-release Pyridostigmine (Duphar) in Healthy Men"

The clinical portion was conducted between March 28, 1988 and April 30, 1988 and draft task reports were being prepared and revised. Several drafts were sent to Col. Schuster and his associates for review, and their suggestions were incorporated into subsequent drafts.

4. Task Order #10

Title: "Multiple-dose Pharmacokinetics, Safety and Tolerance of WR 6026 Hydrochloride in Healthy Subjects"

The clinical portion of this project was initiated on August 16, 1988 and had just recently been completed on December 16, 1988. The data were collected and the analysis continued in preparation for drafting the task report. A

summary of the clinical experiences of the subjects in this study was prepared at the request of Col. Schuster and provided to him in April 1989. An interim report was submitted in June 1989. Unused preparations of study drug were returned.

5. Task Order #11

Title: "Safety, Tolerance, Pharmacokinetics and Pharmacodynamics of Single Oral Doses of Pyridostigmine Administered by an Osmotic-delivery Module (Osmet[®]) Compared to Pyridostigmine Syrup in Healthy Men"

The clinical portion of this project, which began on January 8, 1989, had been completed just prior to this reporting period on February 3, 1989. The data were collected and analysis continued in preparation for drafting the task report.

6. Task Order #12

Title: "Safety, Tolerance, Pharmacokinetics and Pharmacodynamics of Single Oral Doses of a Commercial Formulation of Sustained-release Pyridostigmine in Healthy Men"

The clinical portion of this project, which began on December 12, 1988, had recently been completed on December 23, 1988. The data were collected and analysis continued in preparation for drafting the task report.

7. Task Order #13

Title: "A Protocol to Assess the Irritancy, Contact Sensitization and Contact Photoallergic Potential of Niclosamide - A Topical Anti-schistosomal Agent"

The protocol was developed for this project according to the provisions of Task Order #6 ("Administrative Task Order") during this period. This protocol development involved substantial collaboration with Col. Schuster and others at the Division of Experimental Therapeutics at Walter Reed and individuals of Ft. Detrick, MD.

This task order was initiated by the United States Army Medical Research and Development Command (USAMRDC) on April 20, 1989. A budget was submitted to Contract Specialist Maxine Losee on May 10, 1989. The Task Order was fully executed by Contracting Officer Danny L. Laspe on August 31, 1989. Institutional Review Board (IRB) approvals were granted on October 30, 1989 and on November 3, 1989 by the Johns

Hopkins Joint Committee on Clinical Investigation (JCCI) and the Surgeon General's Human Subjects Research Review Board (HSRRB), respectively. The final technical approval was granted on November 21, 1989. Modification #1 of Task Order #13, extending the performance period to July 31, 1990, was fully executed on February 21, 1990.

The clinical portion of this study was initiated on December 21, 1989 and completed on July 20, 1990. Twenty subjects completed the irritancy threshold phase of the study and 25 subjects completed the contact sensitization and photo-allergenicity portion. Throughout this project the positive and helpful collaboration with Army personnel continued. A preliminary report of the irritancy threshold of niclosamide was issued on March 28, 1990.

8. Task Order #14

Title: "Safety, Tolerance, Pharmacokinetics and Pharmacodynamics of Intravenous Pyridostigmine and Oral Doses of Standard and Sustained-release Pyridostigmine in Healthy Men and the Influence of Food on Oral Pyridostigmine Pharmacokinetics"

The protocol for this study was developed during this reporting period according to the provisions of Task Order #6. This protocol development involved substantial collaboration and review with Col. Schuster and other individuals at the Division of Experimental Therapeutics at Walter Reed.

This task order was initiated by the USAMRDC on June 16, 1989. A budget was submitted to Contract Specialist Maxine Losee on July 11, 1989. The Task Order was fully executed by Contracting Officer Danny L. Laspe on August 31, 1989. IRB approvals were granted on September 26, 1989 and on February 14, 1990 by the JCCI and the HSRRB, respectively. Modification #1 of Task Order #14, extending the performance period to July 31, 1990, was fully executed on February 22, 1990.

The clinical portion of this study was initiated on March 11, 1990 and completed on May 26, 1990. Sixteen subjects successfully completed the study. The collection and analysis of the data began in preparation for drafting the task report.